REMARKS

I. OVERVIEW

Applicants have reviewed and considered the Office Action dated September 22, 2004 and the references cited therewith. Claims 1-10 are now pending in this Application. Applicants respectfully request reconsideration of the above-identified Application in view of the Amendments above and the remarks that follow.

II. CLAIM REJECTIONS - 35 U.S.C. § 112, FIRST PARAGRAPH

Claims 1, 5, 7, and 9 are rejected under 35 U.S.C. § 112, first paragraph, because the Specification, while being enabling for xylitol, does not reasonably provide enablement for any non-ionic osmolyte with low transepithelial permeability. The Examiner refers to the factors as have been described In re Wands, 8 USPQ2d 1400 (Fed. Cir. 1988). The Examiner states that the Specification provides no guidance to enable one of ordinary skill in the art to use the invention commensurate in scope with the claims, which, as stated above, are broad and encompass numerous compounds that may be non-ionic osmolyte with low transepithelial permeability. In re Dreshfield, 110 F.2d 235, 45 U.S.P.Q. 36 (CCPA 1940), gives this general rule. It is well settled in cases involving chemicals and chemical compounds, which differ radically in their properties, and must appear in an applicant's specification either by the enumeration of a sufficient number of the members of a group or by other appropriate language, that the chemicals or chemical combinations included in the claims are capable of accomplishing the desired result. The Examiner states that Applicants' specification does not set forth a representative number of examples of non-ionic osmolytes with low transepithelial permeability, which would be capable of performing the claimed methods.

Applicants respectfully traverse this rejection. The test for enablement under § 112, first paragraph, "whether or not the specification contains a sufficiently explicit disclosure to enable one having ordinary skill in the relevant field to practice the invention claimed therein without the exercise of undue experimentation." Ex parte Foreman, 230 U.S.P.Q. 546 (Bd. Pat. App. & Int'f. 1986). Applicants respectfully submit that the specification in the instant invention does provide other non-ionic osmolytes with a low permeability. The specification states that "[x]ylitol is not the only agent that can be used; studies demonstrate that other non-ionic osmolytes affecting low transepithelial permeability might be effective." Specification, at page 16. Further, the "osmolytes should not provide a ready carbon source for bacterial growth and be safe in humans" in order to be effective. Specification, at page 16. It is important to note that one ordinarily skilled in the art would know that an osmolyte is a compound that protects cells from desiccation by meeting high intracellular osmality. Further, compounds that are known as osmolytes include polyols (polyhydric alcohol), amines, certain amino acids, and urea (see dictionary cite www.xrefer.com). Applicants emphasize that the specification thereby does set forth a representative number of examples of non-ionic osmolytes which would be capable of performing the claimed methods and would be enabling for one skilled in the art.

Applicants further submit that an osmolyte with lower transepithelial permeability is also enabled by the specification. The use of these terms in conjunction are known to those in the art that a low transepithelial permability teaches the process by which an osmolyte moves through the epithelium with relatively low permeability thereby allowing for the osmolyte to temporarily hold liquid on the apical surface and thereby reduce the rate of a liquid absorption. Specification, at page 29. For example, in cystic fibrosis the disease is caused by a mutation in the gene ending the cystic fibrosis transmembrane conductance regulator (CFTR) which is a unique chloride (Cl^-)

channel located in the apical membrane of epithelia, where it mediates transepithelial cells and liquid movement. Therefore, the use of an osmolyte which is relatively non-permeable reduces the absorption rate and holds the liquid on the apical surface allowing the sodium chloride (NaCl) concentration to decrease which enhances bacterial killing by endogenous antimicrobial factors. Specification, at page 32. The Applicants have discovered that the use of osmolyte administration to the airway surface is of substantial value "preventing or delaying the onset of cystic fibrosis respiratory track infections". Specification, at page 12.

In addition, Applicants submit that there is adequate direction how to utilize these materials and methods described in the specification to be enabling for one skilled in the art to practice the invention. Applicants teach that in order to evaluate the effect of an osmolyte on bacterial killings by endogenous antimicrobial factors, a luminescence assay is utilized. Specification, at page 25. The luminescence assay is enabled by the specification and provides sufficient guidance to one skilled in the art. Specification, at pages 25 and 31. The use of this assay and the known osmolytes that can be used to perform the claimed invention as stated above, does provide the requisite teachings to enable one skilled in the art to perform the claimed methods. The Examiner states that In re Dreshfield provides a general rule whereby "chemicals and compounds, which differ radically in their properties, must appear in an applicant's specification either by the enumeration of a sufficient number of members of a group or by other appropriate language." In re Dreshfield, 45 U.S.P.Q. 36 (CCPA 1940). Applicants assert that not only have a representative number of osmolytes been disclosed as discussed above, but also for the use of luminescence assay is taught in order to accomplish the desired results.

Based on the foregoing, Applicants respectfully submit that the specification does provide enablement commensurate with the scope of claims 1-10. Thus Applicants respectfully request

the rejections to claims 1-10 under 35 U.S.C. § 112, first paragraph be withdrawn and reconsidered.

III. CLAIM REJECTIONS - 35 U.S.C. § 102(b)

A. Claims 1-4, and 7-8 are rejected under 35 U.S.C. § 102(b) as being anticipated by Uhari et al., 5,719,196. The Examiner states that Uhari et al. disclose methods of treating or preventing "infections such as otitis media, upper respiratory infections, acute bronchitis, sinusitis and conjunctivitis, the methods comprising orally administering (tablets, powders or lozenges) effective amounts of xylitol." The Examiner further states that Uhari et al. teach "that the xylitol exhibits a growth inhibiting effect again pneumococci".

Applicants respectfully traverse this rejection. The cited reference does not disclose nor suggest a method for lowering ionic strength in body fluids whereby the application of low permeability, non-ionic osmolytes allows endogenous antimicrobials to cure infectious microbial cells without ingestion or minimal absorption of the osmolyte into the airway surface liquid (ASL) as in the present invention. Specification, at page 10. Claim 1 of the present invention recites a method of exposing infectious microbial cells to endogenous antimicrobials. In addition, claims 1, 4 and 7 do not refer to pneumococci as suggested in the cited reference. The distinct differences between the *Streptococcus* species in the cited reference and the endogenous bacteria of the claimed invention, including *Staphylococcus* and *Pseudomonas*, are well known to one skilled in the art. In addition, Uhari et al. teach a method of treating respiratory infections through the use of solely oral administration in the form of a solid preparation such as chewing gum. '196, column 5, lines 12-15. The cited reference more specifically teaches the use of oral administration to prevent acute otitis media whereby xylitol is actually transported into the cells

through absorption and thus ingested through the chewing of gum. '196, column 1, lines 22-25. The present invention instead affects the permeability of the thin layer of liquid covering the airway surface (ASL) which contains many anti microbial substances. These substances acting alone and synergistically form part of the local pulmonary host defense system. However, in compromised physical states, such as cystic fibrosis, their activity is impaired because of the loss of CFTR Cl^- channels that lead to a higher ASL salt concentration, which reduces antimicrobial potency and thereby impairs the innate immune system. Specification, at page 12. In addition, the claims specifically teach a low permeability of the epithelium thereby an extremely minimal absorption of xylitol and no ingestion through the epithelium. See claims 1, 4 and 5. Applicants submit that the present invention is clearly not anticipated by Uhari et al. Uhari et al. not only does not suggest the lowering of ionic strength thereby providing greater bacterial killing but the cited reference also does not teach the administration of the claimed non-ionic osmolyte which is not ingested nor absorbed into the patient providing less immune response, complications and a quicker delivery than the solid preparation of Uhari et al.

In light of the above remarks, Applicants respectfully submit that the reference cited by the Examiner does not teach, or suggest the unique method of killing infectious microbial cells, lowering ionic strength of body fluids or prevention, and/or treatment of epithelial infections. Therefore, independent claims 1, 4 and 7 are not anticipated by Uhari et al. Claims 2-3, dependent on claim 1, and claim 7, dependent on claim 8, are likewise not anticipated by Uhari et al since they recite similar elements as claims 1, 4 and 7 and are patentable over Uhari for similar reasons as those argued above, plus the elements in the claims. Applicants respectfully request reconsideration and withdrawal of the rejections to claims 1-4 and 7-8 under 35 U.S.C. § 102(b).

B. Claims 5-6 stand rejected under 35 U.S.C. § 102(b) as being anticipated by Franz et al. Patent No. 5,527,831. The Examiner states that Franz et al. disclose a method of treating interocular pressure by topically administering to the eye of an individual in need of treatment an effective amount of a composition comprising xylitol. '831, column 4, lines 10-20. The Examiner states that the claims are anticipated by Franz et al. because Franz et al. disclose administration of an identical agent, i.e., xylitol, to a host using Applicant's claimed method steps. The Examiner states that a reduction in the ionic strength of surface fluid leading to antimicrobial activity against infectious cells is an inherent characteristic of the method.

Applicants respectfully traverse this ground of rejection. Applicants respectfully submit that the Office Action did not make out a *prima facie* case of anticipation for the following reasons: (1) the reference does not teach each and every claim element and (2) the reference does not teach the identical invention in as complete detail as is contained the claim.

Anticipation requires the disclosure in a single prior art reference of each element of the claim under consideration. *In re Dillon* 919 F.2d 688, 16 USPQ2d 1897, 1908 (Fed. Cir. 1990) (en banc), cert. denied, 500 U.S. 904 (1991).

Claim 5 recites: "administering to an external eye an effective amount of a non-ionic osmolyte, wherein said external eye has a fluid containing endogenous antimicrobials, thereby reducing the strength of said fluid...promoting antimicrobial activity against infectious cells." In contrast, Franz et al simply describe "administering to the eye of said host an ophthalmic solution comprising a quantity of a polyhydroxyalcohol." ('831, claim 1). Thus, the Franz reference does not teach each element of claim 5 because the method in Franz treats an eye that has increased intraocular eye pressure of aqueous humor, rather than Applicants' method that treats an infected

eye by promoting antimicrobial activity against infectious cells using a non-ionic osmolyte. Specification, at page 19.

Moreover, Franz does not teach the reduction of ionic strength with a low permeability non-ionic osmolyte for the prevention or treatment of infection by promoting antimicrobial activity against infectious cells as in claim 5 or as taught in the specification. Specification, at page 19. Further, the cited reference only teaches the use of the xylitol solution for the treating of increased intraocular pressure. '831, column 2, lines 31-36. In contrast the present invention teaches the treatment and prevention of infectious microbial cells, by enhancing the main antibacterial defense system. Specification, at page 12.

Second, the Office Action also failed to make a prima facie case because "[t]he identical invention must be shown in as complete detail as is contained in the ... claim." *Richardson v. Suzuki Motor Co.*, 868 F.2d 1226, 1236, 9 USPQ2d 1913, 1920 (Fed. Cir. 1989); MPEP § 2131.

Claim 5 recites: "administering to an external eye an effective amount of a non-ionic osmolyte, wherein said external eye has a fluid containing endogenous antimicrobials, thereby reducing the strength of said fluid ...promoting antimicrobial activity against infectious cells." In contrast, Franz et al describe administering to the eye of said host an ophthalmic solution comprising a quantity of a polyhydroxyalcohol." ('831, claim 1). Thus, the Franz reference does not teach the identical invention in as complete detail as is contained in claim 5.

Moreover, Franz does not teach the reduction of ionic strength with a low permeability non-ionic osmolyte for the prevention or treatment of infection by promoting antimicrobial activity against infectious cells as in claim 5 or as taught in the specification. Specification, at page 19. Further, the cited reference only teaches the use of the xylitol solution for the treating of increased intraocular pressure. '831, column 2, lines 31-36. In contrast the present invention

teaches the treatment and prevention of infectious microbial cells by enhancing the main antibacterial defense system. Specification, at page 12.

Applicants respectfully submit that the reference cited by the Examiner does not teach, or suggest the unique method of killing infectious microbial cells, lowering ionic strength of body fluids or treatment of eye infections. Therefore, claim 5 is not anticipated by Franz et al. Dependent claim 6 recites similar elements as claim 5 and is patentable over Franz for similar reasons as those argued above, plus the elements in the claims. Applicants respectfully request that the rejection of claims 5 and 6 under 35 U.S.C. § 102(b) be withdrawn and reconsidered.

IV. CLAIMS REJECTIONS - 35 U.S.C. § 102 (e)

Claims 1-4 and 7-8 stand rejected under 35 U.S.C. § 102(e) as being anticipated by Jones, Patent No. 6,054,143. The Examiner states that Jones discloses a method of treating or presenting upper respiratory infection such as otitis media and sinusitis by nasally administering effective amounts of xylitol."

Applicants respectfully traverse this rejection. The Jones reference simply provides a general disclosure of a means of cleaning the nasopharynx to reduce the population of pathogenic bacteria through nasal administration of a xylitol solution. Jones does not teach the reduction of ASL ionic strength with a low permeability non-ionic osmolyte for the prevention or treatment of infection by any of the infectious microbes for which the endogenous antimicrobials as in claim 1 or as taught in the specification. Specification, at page 19. Further, the cited reference only teaches the use of the nasally administered xylitol solution for the cleaning of the nasopharynx once it has become irritated. '143, column 2, lines 13-14. In contrast the present invention teaches the treatment and prevention of infectious microbial cells, such as respiratory infections by enhancing the main antibacterial defense system through administration via an aerosol or powder. Specification, at page 5. See also claims 1-4, and 7-8. In addition, the cited reference

teaches that the bacteria are not killed but rather infections are reduced. '143, column 2, line 34. The present invention teaches away from this. In fact, Applicants teach the killing of infectious microbial cells in claim 1 by exposing the infectious cells to non-ionic osmolytes thereby lowering the ASL sodium chloride concentration level increase the activity of endogenous antimicrobials. Specification, at page 12.

In addition, Applicants respectfully submit that "for prior art to anticipate under 35 U.S.C. § 102, every element of the claimed invention must be identically disclosed, either expressly or under principles of inherency in a single reference." Sumitomo Electric, 9 U.S.P.Q.2d 1962, 1965 (Fed. Cir. 1989). The exclusion of a claimed element, no matter how insubstantial or obvious from a prior art reference is enough to negate anticipation. Id. In order to be anticipated there must be a teaching of a viral, as opposed to a bacterial of a mammalian protein, properly folded (glycosylated) and finally that it expresses at adequate levels. Ex parte Duels, 33 U.S.P.Q.2d 1445, 1451 (Bd. Pat. App. & Int'l 1993). This teaching cannot come from Applicant's own specification. Id. Thus Jones does not provide sufficient description to one skilled in the art to practice the Applicant's invention.

Applicants respectfully submit that the reference cited by the Examiner does not teach or suggest the claimed invention. Therefore, independent claims 1, 4 and 7 are not anticipated by Jones et al. Claims 2-3, dependent on claim 1, and claim 7, dependent on claim 8, are likewise not anticipated by Jones et al since they recite similar elements as claims 1, 4 and 7 and are patentable over Jones for similar reasons as those argued above, plus the elements in the claims. Applicants respectfully request reconsideration and withdrawal of the rejections to claims 1-4 and 7-8 under 35 U.S.C. § 102(e).

V. CLAIM REJECTIONS - 35 U.S.C. § 102(a)

Claims 9-10 stand rejected under 35 U.S.C. § 102(a) as being anticipated by WO 99/27922. Examiner states that '922 teaches a method for treating vaginal yeast infections,

wherein the method comprises topically administering to the vagina an effective amount of a composition containing xylitol. '922, page 7, lines 5-8. Examiner further states that the claims are anticipated by '922 because '922 discloses administration of an identical agent, i.e., xylitol, to host using Applicant's claimed method steps. The Examiner states that a reduction in ionic strength of surface fluid leading to antimicrobial activity against infectious cells is an inherent characteristic of the method.

Applicants respectfully traverse this ground of rejection. Applicants respectfully submit that the Office Action did not make out a *prima facie* case of anticipation for the following reasons: (1) the reference does not teach each and every claim element and (2) the reference does not teach the identical invention in as complete detail as is contained the claim.

Anticipation requires the disclosure in a single prior art reference of each element of the claim under consideration. *In re Dillon* 919 F.2d 688, 16 USPQ2d 1897, 1908 (Fed. Cir. 1990) (en banc), cert. denied, 500 U.S. 904 (1991).

Claim 9 recites "administering to a vaginal surface an effective amount of a non-ionic osmolyte, wherein said surface has a fluid containing endogenous antimicrobials, thereby reducing the ionic strength of said fluid containing said endogenous antimicrobials and promoting antimicrobial activity against infectious cells." In contrast, '922 simply describes that "xylitol may thus be included in a cream, jelly, lubricant, or liquid or it may preferably be applied onto the surface of a condom" to treat a yeast infection. '822, Specification, at page 7, lines 5-8. Thus, the '922 reference does not teach each element of claim 9 because the method described in '922 treats a yeast infection, in contrast to Applicants' method that treats infectious microbial cells in the vagina using a unique method to enhance antimicrobial activity.

The '922 patent does not teach the reduction of ionic strength with a low permeability non-ionic osmolyte for the prevention or treatment of infection by promoting antimicrobial activity against infectious cells as in claim 9 or as taught in the specification. Specification, at page 19. Further, the cited reference only teaches the use of the xylitol solution for the treating yeast infection. '922, page 7, lines 5-8. In contrast the present invention teaches the treatment and prevention of infectious microbial cells, by enhancing the main antibacterial defense system. Specification, at page 12.

Second, the Office Action also failed to make a prima facie case because "[t]he identical invention must be shown in as complete detail as is contained in the ... claim." *Richardson v. Suzuki Motor Co.*, 868 F.2d 1226, 1236, 9 USPQ2d 1913, 1920 (Fed. Cir. 1989); MPEP § 2131.

Claim 9 recites "administering to a vaginal surface an effective amount of a non-ionic osmolyte, wherein said surface has a fluid containing endogenous antimicrobials, thereby reducing the ionic strength of said fluid containing said endogenous antimicrobials and promoting antimicrobial activity against infectious cells." In contrast, '922 simply describes that "xylitol may thus be included in a cream, jelly, lubricant, or liquid or it may preferably be applied onto the surface of a condom" to treat a yeast infection. '922, at page 7, lines 5-8. Thus, the '922 reference does not teach each element of claim 9 because the method described in '922 treats a yeast infection, rather than Applicants' method that treats infectious microbial cells in the vagina using a unique method.

The '922 patent does not teach the reduction of ionic strength with a low permeability non-ionic osmolyte for the prevention or treatment of infection by promoting antimicrobial activity against infectious cells as in claim 9 or as taught in the specification. Specification, at page 19. Further, the cited reference only teaches the use of the xylitol solution for the treating

of vaginal yeast infections. '922, at page 7, lines 5-8. In contrast the present invention teaches the treatment and prevention of infectious microbial cells, by enhancing the main antibacterial defense system. Specification, at page 12.

'922 does not teach the reduction of ionic strength with a low permeability non-ionic osmolyte for the prevention or treatment of infection by any of the infectious microbes for which the endogenous antimicrobials as in claim 9 or as taught in the specification. Specification, at page 19. Further, the cited reference only teaches the use of the xylitol solution for the treating of vaginal yeast infection. '922, at page 7, lines 5-8. In contrast the present invention teaches the treatment and prevention of infectious microbial cells, by enhancing the main antibacterial defense system. Specification, at page 12. Thus, the '922 patent does not teach the identical invention in as complete detail as is contained in claim 9.

Applicants submit that the present invention is clearly not anticipated by '922. The '922 patent does not suggest the lowering of ionic strength thereby providing greater antimicrobial killing. Therefore, claim 9 is not anticipated by '922. Dependent claim 10 recites similar elements as claim 9 and is patentable over '922 for similar reasons as those argued above, plus the elements in the claims. Applicants respectfully request that the rejection of claims 5 and 6 under 35 U.S.C. § 102(a) be withdrawn and reconsidered.

VI. DOUBLE PATENTING REJECTION

Claims 1-4 and 7-8 were rejected under judicially created doctrine of obviousness type double patenting as being unpatentable over claims 1-16 of U.S. Patent No. 6,716,819. A Terminal Disclaimer is enclosed herewith to obviate the double patenting rejection.

VII. CONCLUSION

This is also a request to extend the period for filing a response in the above-identified application for one-month from December 22, 2004 to January 22, 2005. Applicant is a small entity; therefore, please charge Deposit Account No. 26-0084 in the amount of $60.00 to cover the cost of the one-month extension. Any deficiency or overpayment should be charged or credited to Deposit Account 26-0084.

Reconsideration and allowance is respectfully requested.

Respectfully submitted,

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